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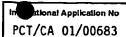
For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

087343 A3

(54) Title: COMBINATION THERAPY USING COX-2 SELECTIVE INHIBITOR AND THROMBOXANE INHIBITOR AND COMPOSITIONS THEREFOR

(57) Abstract: The present invention provides a method for the treatment or prophylaxis of COX-2 mediated conditions in patients who are at risk of developing thromboembolic events which comprises administering to said patient a therapeutically or prophylactically effective amount of a COX-2 selective inhibitor and a cardiovascular protective amount of a thromboxane inhibitor, as well as compositions therefor.

INTERNATIONAL SEARCH REPORT



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A. CLASSI IPC 7	FICATION OF SUBJECT MATTER A61K45/06 A61P35/00 A61P25/2	28 A61P19/02	A61P9/00								
According to International Patent Classification (IPC) or to both national classification and IPC											
B. FIELDS	SEARCHED										
Minimum do IPC 7	cumentation searched (classification system followed by classification $A61K$	ion symbols)									
	ion searched other than minimum documentation to the extent that s										
· ·	ata base consulted during the international search (name of data ba		terms used)								
EPO-Internal, CHEM ABS Data, BIOSIS, EMBASE											
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT										
Category *	Chatlon of document, with indication, where appropriate, of the rel	evant passages	. Relevant to claim No.								
X	WO 98 50033 A (LUNDY KRISTIN MARI ;RICKETTS ANTHONY PAUL (US); PFIZ 12 November 1998 (1998-11-12) claims 1,4,11	1,2									
X	WO 00 23061 A (DEMOPULOS GREGORY JEFFREY M (US); PALMER PAMELA P (27 April 2000 (2000-04-27) claims 1,3,14		1,2,11								
Further documents are listed in the continuation of box C. X Patent family members are tisted in annex.											
* Special categories of cited documents: The intermediate in the continuation of box C. The intermediate is seed in annex.											
A document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filling date *L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filling date but later than the priority date claimed *Coursent referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filling date but later than the priority date claimed *Coursent referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filling date but later than the priority date claimed *Coursent of particular relevance; the claimed invention cannot be considered novel or cannot be co											
Date of the actual completion of the international search Date of mailing of the international search report											
	July 2002	16/07/2002									
Name and n	nailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Leherte, C									

INTERNATIONAL SEARCH REPORT

international application No. PCT/CA 01/00683

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of Iirst sheet)
This international Search Report has not been established in respect of certain dalms under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 111 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. X Claims Nos.: 1-16 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.
The protest description and payment of decinoring sources recom-

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-16

Present claims 1-16 relate to compounds and therapeutic applications defined (inter alia) by reference to the following parameters: "COX-2 selective inhibitor", "cardiovascular protective amount of a thromboxane inhibitor" and "COX-2 mediated conditions".

The use of these parameters in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is impossible to compare the parameters the applicant has chosen to employ with what is set out in the prior art. The lack of clarity is such as to render a meaningful complete search impossible. Consequently, the search has been restricted to combinations of the COX-2 selective inhibitors individually structurally identified by name in the claims and the thromboxane inhibitors individually structurally identified by name on page 16 and 17 of the description, with due regard to the specified therapeutic applications mentioned in the claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

information on patent family mempers

In ational Application No
PCT/CA 01/00683

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9850033	A	12-11-1998	AU	6932198 A	27-11-1998
			BG	103852 A	30-06-2000
			BR	9808720 A	11-07-2000
			CN	1255059 T	31-05-2000
			EP	0988034 A1	29-03-2000
			HR	980244 A1	28-02-1999
			HU	0001286 A2	28-11-2000
			WO	9850033 A1	12-11-1998
			JP	2000513020 T	03-10-2000
			NO	995389 A	04-01-2000
			NZ	500183 A	26-04-2002
			PL	337003 A1	31-07-2000
			SK	148199 A3	11-09-2001
			ZA	9803722 A	04-11-1999
WO 0023061	Α	27-04-2000	AU	1214800 A	08-05-2000
			WO	0023061 A2	27-04-2000
			US	2002028798 A1	07-03-2002